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Outcome of patients over 80 years of age on prolonged suppressive antibiotic therapy for at least 6 months for prosthetic joint infection

Virginie Prendki [a,b,c,*], Valérie Zeller [b,c,d], Dorick Passeron [c,d], Nicole Desplaces [c,e], Patrick Mamoudy [c,d], Jérôme Stirnemann [a], Simon Marmor [c,d], Jean-Marc Ziza [b,c]

[a] Department of Internal Medicine, Rehabilitation and Geriatrics, Hôpitaux Universitaires de Genève, Hôpital des Trois-Chêne, Chemin de Pont Bochet, 1226 Thônex, Switzerland
[b] Department of Internal Medicine and Rheumatology, Groupe Hospitalier Diaconesses Croix Saint Simon, Paris, France
[c] Centre de Référence pour les Infections Ostéo Articulaires Complexes, Groupe Hospitalier Diaconesses Croix Saint Simon, Paris, France
[d] Department of Orthopaedic Surgery, Groupe Hospitalier Diaconesses Croix Saint Simon, Paris, France
[e] Biological Laboratory, Groupe Hospitalier Diaconesses Croix Saint Simon, Paris, France

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SUMMARY

Objectives: To describe elderly patients treated with prolonged suppressive antibiotic therapy for a prosthetic joint infection (PJI) in cases where the infected prosthesis could not be removed.
Methods: All patients aged ≥80 years with a documented PJI and treated with prolonged suppressive antibiotic therapy for more than 6 months were included retrospectively in this study. The following events were noted: failure including persisting infection, relapse, new infection, treatment discontinuation due to severe adverse events, and related death, and also unrelated death.
Results: Thirty-eight patients with a median age of 84 years (80–95 years) were included; there were 24 hip infections, 13 knee infections, and one shoulder infection. The main causative organisms were *Staphylococcus aureus* (39%) and *Streptococcus agalactiae* (16%). The most commonly prescribed antibiotics as prolonged suppressive therapy were penicillins. The median follow-up duration was 24 months; 60% of the patients were event-free at 24 months and were still on prolonged suppressive antibiotic therapy. Fifteen events (six failures and nine unrelated deaths) were observed. Hypoalbuminaemia, the presence of a sinus tract, and a staphylococcal PJI were associated with an increased risk of an event.
Conclusions: Prolonged suppressive antibiotic therapy is an alternative therapy in elderly patients with PJI when surgery is contraindicated and when the bacteria are susceptible to well-tolerated oral antimicrobial therapy such as beta-lactams.

1. Introduction

Infection is the most dramatic complication of arthroplasties, which are used widely nowadays, especially in the elderly.[1–3] In France, approximately 100 000 total hip arthroplasties (THA) and 40 000 total knee arthroplasties (TKA) are implanted every year, with an infection incidence of 1–2% for THA and 3% for TKA.[4] In the USA, over 500 000 primary arthroplasties are implanted every year and over one million people currently live with a prosthetic joint.[5] It is anticipated that by 2030 more than four million primary THA and TKA replacements will be done per year.[3] Sixty percent of individuals with a THA in the USA are over 65 years of age and 5% over 85 years; further, 17% of patients with revision hip replacements have at least three comorbidities.[2]

Treatment strategies to cure prosthetic joint infections (PJIs) require removal, one- or two-stage replacement of the prosthesis, and prolonged systemic antibiotic therapy for a total of 3 months.[1,6] Patients with a well-fixed prosthesis, without a sinus tract, and who are within 30 days of prosthesis implantation or <3 weeks of onset of infectious symptoms should be proposed the 'DAIR' strategy of debridement, antibiotics, irrigation, and retention of the prosthesis.[6] Other patients who do not meet these criteria may also be proposed DAIR, or a minimal surgical strategy, or no surgery at all, for example when a prosthesis exchange strategy is unacceptable because of the risks involved and/or patient refusal. In these cases, where relapse of infection is more

* Corresponding author. Tel.: +41 79 553 83 08; fax: +41 22 305 61 15.
E-mail address: virginie.prendki@hcuge.ch (V. Prendki).

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likely, prolonged suppressive antibiotic therapy (PSAT), which is defined as an oral antibiotic therapy prescribed for a duration longer than a curative treatment, may be used for palliative purposes. Its aim is to inhibit bacterial growth around the prosthesis and avoid the dissemination of infection.

Studies on this subject are few and of limited size.[7–10] Most of them included patients treated surgically and did not describe the oldest and frailest patients. Moreover, they did not provide patient demographics including age and treatment indications.

The objective of this study was to describe patients aged 80 years and older for whom surgical excision was contraindicated as a result of medical and surgical conditions or patient refusal, who received PSAT for a PJI for at least 6 months, and to describe their treatment and outcome.

2. Methods

2.1. Study design and population

This retrospective observational study was carried out in a French regional referral centre for osteoarticular infections at the Groupe Hospitalier Diaconesses Croix Saint Simon in Paris. All patients treated from January 2004 to December 2011 were eligible. Cases were identified retrospectively using the registry and medical charts of the orthopaedic department. Patients were included if they were aged ≥80 years and had a microbiologically confirmed PJI, either by joint aspiration or by intraoperative culture. Their prosthesis was not removed and they were treated with suppressive antibiotic therapy for at least 6 months.

The following data were collected: sex, age, medical history, past history of PJI, ASA score (American Society of Anesthesiologists), symptoms of PJI (fever, pain, fistula), type of PJI (acute or chronic, postoperative or haematogenous), and the pathogen isolated.

2.2. Prolonged suppressive antibiotic therapy

Indications for PSAT were collected and classified as very high operative risk, very complex surgical intervention, or patient refusal. The antibiotic therapy was detailed, including (1) the initial intravenous antibiotic therapy and the following oral regimen, which included the initial higher doses (considered as curative treatment) and the subsequent lower doses, (2) the duration of treatment, and (3) drug-related adverse events and reasons for drug withdrawal. The duration of PSAT included the initial intravenous treatment. Doses were prescribed according to the national recommendations of France.[11]

2.3. Surgery

Patients underwent surgery only to drain an abscess, to reduce the bacterial burden, or to perform a partial exchange in those with severe pain and loosened components. The indications and types of intervention were recorded.

2.4. Outcome

Patients were seen as outpatients every 3 to 6 months. For patients not seen for more than 1 year, they or their referring doctor was contacted by phone. The following events were noted: treatment failure including persisting infection, relapse, new infection, treatment discontinuation because of severe adverse events, or related death. Unrelated death was included in events.

2.5. Definitions

PJI was defined as a sinus tract communicating with the prosthesis or clinical (local inflammatory signs including swelling, warmth, erythema), laboratory (C-reactive protein (CRP) >5 mg/l), or radiological signs (periosteal bone formation, subchondral osteolysis) of infection, and positive cultures of joint fluid aspiration and a synovial leukocyte count $>4.300 \times 10^9$/l with a differential of >80% neutrophils in hip infection, or a synovial leukocyte count $>1.700 \times 10^9$/l with a differential of >65% neutrophils in knee infection, or isolation of the same organism from two or more cultures of intraoperative tissue specimens.

Acute infection was defined as a duration of symptoms less than 1 month. Early infection was considered if it occurred within 1 year after surgery (corresponding to time free of symptoms).

Persisting infection was defined as persistence of clinical signs of PJI. Reappearance of clinical signs of PJI after a symptom-free period led to the diagnosis of 'relapse' if the same bacterial organism was isolated as was found at inclusion, or as 'new infection' if the organism was different.

2.6. Statistical analysis

Statistical analyses were performed with R (version 2.10.1) software. A Kaplan–Meier curve was generated to assess overall survival without an event. Factors related to the occurrence of an event were analyzed with a univariate log-rank test, and the unadjusted hazard ratio (HR) was performed with Cox analysis for each factor. The level of significance was set at $p < 0.05$.

3. Results

3.1. Patients

A total of 452 patients were treated for PJI during the study period, 104 of whom were ≥80 years old. Of these, 38 patients were included in the study, i.e., 8% of all patients and 36.5% of patients aged ≥80 years. Their characteristics are detailed in Table 1. The median duration of symptoms was 99 days (range 1–1825 days). Fifteen patients had an acute infection and 15 an early-onset infection. The infection was classified as postoperative in 23 patients. Among these, the portal of entry was cutaneous in seven patients, dental in three, urinary in three, digestive in three, and undetermined in two. Two patients had endocarditis confirmed by echocardiography, including one with pacemaker-related endocarditis. The other patient had concomitant cervical spondylodiscitis.

3.2. Microbiology

The microorganisms isolated in these patients are shown in Table 2. Identification was done by joint aspiration in 29 patients (76%) and by intraoperative cultures in nine patients.

3.3. Prolonged suppressive antibiotic therapy

Indications for PSAT were a very high operative risk for 20 patients, a very complex surgical intervention for nine, and patient refusal to have surgery for nine.

Thirty-two patients initially received an intravenous (IV) antibiotic therapy for a median duration of 30 days (range 10–45 days) prior to the oral regimen. The IV agents used were beta-lactams in 24 patients (amoxicillin in 10, cefazolin in 10, ceftriaxone in two, and cloxacillin in two), clindamycin in four, and vancomycin in four. They were associated with aminosides for less than 1 week in 20 patients and with rifampin in 15 patients with susceptible *Staphylococcus aureus* infections.

Table 1
Baseline characteristics of 38 patients with prosthetic joint infections treated with prolonged suppressive antibiotic therapy

Characteristics	
Gender, male, *n* (%)	17 (45)
Age, years, median (range)	84 (80–95)
BMI, kg/m^2, median (range)	26 (15.8–33.3)
Difficulty walking, *n* (%)	17 (45)
Bedsores, *n* (%)	3 (8)
Medical co-morbidity, *n* (%)	36 (95)
Cardiovascular disease,[a] *n* (%)	32 (84)
Chronic renal failure, *n* (%)	7 (18)
Long-term oral corticosteroids, *n* (%)	4 (11)
Malignancy within the last 5 years, *n*	3
Chronic dermatitis, *n*	3
Alzheimer's disease, *n*	1
Insulin-requiring diabetes, *n*	1
Rheumatoid arthritis, *n*	1
Previous PJI, *n* (%)	14 (37)
ASA score of 3, *n* (%)	21 (55)
Site of PJI, *n* (%)	
Hip	24 (63)
Knee	13 (34)
Shoulder	1
Description of the infection, *n* (%)	
Early	15 (39%)
Acute	15 (39%)
Postsurgical	23 (61%)
Physical examination, *n* (%)	
Fever	14 (37)
Sinus tract	9 (24)
Laboratory examination	
Total leukocyte count, $\times 10^9$/l, median (range)	8.820 (5.400–18.950)
CRP, mg/l, median (range)	74 (2–600)
Serum albumin, g/l, median (range)	29 (17–41)

BMI, body mass index; PJI, prosthetic joint infection; ASA, American Society of Anesthesiologists; CRP, C-reactive protein.
[a] Cardiovascular disease: arterial hypertension (*n* = 15), cardiac arrhythmia (*n* = 14; two patients with a pacemaker), coronary heart disease (*n* = 6; two patients with a coronary bypass), valvular disease (*n* = 4), venous thromboembolic disease (*n* = 5), ischaemic stroke (*n* = 4), peripheral arterial disease (*n* = 4).

High-dose oral agents were prescribed after IV therapy for 27 patients for a median duration of 45 days (range 15–60 days). Eleven patients received a single-agent regimen and 16 a combination of two effective oral antimicrobials. Drugs used were amoxicillin (8), amoxicillin–clavulanate (1), cloxacillin (4), clindamycin (7), co-trimoxazole (1), fusidic acid (5), minocycline (1), levofloxacin (1), peflacin (2), and rifampin (13). Curative treatment was prescribed for a median duration of 59 days (range 15–90 days).

The oral agents used at lower doses are detailed in Table 3; all patients received a single-agent regimen.

Table 2
Bacterial pathogens isolated in 38 prosthetic joint infections treated with prolonged suppressive antibiotic therapy

Pathogen	*n* (%)	Event (failure)
Staphylococcus species	20 (53)	11 (6)
Staphylococcus aureus	15 (39)	10 (5)
Methicillin-sensitive	10	5 (3)
Methicillin-resistant	5	5 (2)
Coagulase-negative staphylococci[a]	5	1 (1)
Streptococcus species	7 (18)	1
Streptococcus agalactiae	6 (16)	1
Streptococcus salivarius	1	0
Enterococcus species	2	0
Enterococcus faecalis	2	0
Gram-negative bacilli	5 (13)	1
Enterobacteriaceae[b]	2	0
Campylobacter fetus	3	1
Anaerobic bacteria	4 (11)	2 (1)
Propionibacterium acnes	3	1
Finegoldia magna	1	1 (1)
Bacteraemia[c]	9 (24)	4 (2)
Endocarditis[d]	2 (5)	1 (1)

[a] *Staphylococcus epidermidis* (*n* = 2), *Staphylococcus lugdunensis* (*n* = 2), unidentified coagulase-negative Staphylococcus (*n* = 1).
[b] *Citrobacter koseri* (*n* = 1), *Enterobacter cloacae* (*n* = 1).
[c] *Staphylococcus aureus* (*n* = 4), *Streptococcus agalactiae* (*n* = 2), *Enterococcus faecalis* (*n* = 2), *Campylobacter fetus* (*n* = 1).
[d] *Streptococcus agalactiae* (*n* = 1), *Campylobacter fetus* (*n* = 1).

3.4. Surgical interventions

Nine patients underwent surgery, including synovectomy (*n* = 6), abscess drainage (*n* = 3), partial exchange (*n* = 1), and excision of fistula (*n* = 1). The pacemaker could not be removed in the patient with pacemaker-related endocarditis.

3.5. Outcome

A total of 15 events were observed, with a median follow-up duration of 24 months (range 6–98 months). Six failures occurred: one persisting infection, three relapses, one related death, and one treatment discontinuation. The patient who had a persisting infection was infected with methicillin-resistant *S. aureus* (MRSA). She had a sinus tract that persisted under antibiotic therapy, but co-trimoxazole was continued because fever and local inflammation decreased. She finally became bedridden and was institutionalized. Relapses occurred in three patients with methicillin-susceptible *S. aureus* (MSSA) treated with cloxacillin. They were hospitalized and received new anti-staphylococcal intravenous treatment and then another molecule for prolonged suppression (cefazolin before each dialysis session for one patient, clindamycin for the others). None of these patients underwent new surgery and their outcome was favourable. The infection-related death occurred in an 84-year-old patient whose prosthesis was infected with *Finegoldia magna*. She was treated with clindamycin but died from septic shock due to a new prosthetic infection. The last patient with failure received prolonged co-trimoxazole for an MRSA infection, which had to be stopped after 4 months of low oral dose because of renal failure and recurrent *Clostridium difficile* colitis. Four more patients experienced reversible adverse events (nausea and mycosis), but could continue their treatment.

Nine patients died of unrelated causes (two from cardiac failure, one from renal failure, one from mesenteric ischemia, one from intestinal obstruction, one from pulmonary embolism, and three from bedsore complications). In a Kaplan–Meier analysis, 60% of the patients were event-free at 24 months and still on PSAT (Figure 1). Their treatment was considered successful. Six out of seven patients with a streptococcal PJI belonged to this group and were treated successfully with amoxicillin, the only event occurring 8 years after the beginning of PSAT from death unrelated to infection.

The results of univariate analysis are presented in Tables 4 and 5. Variables associated with an increased risk of an event were age ≥85 years ($P = 0.016$), female gender ($P = 0.023$), difficulty walking ($P = 0.049$), hypoalbuminaemia ($P = 0.019$), the presence of a sinus tract ($P = 0.020$), and a staphylococcal PJI ($P = 0.01$).

4. Discussion

PSAT is sometimes proposed in patients for whom surgical strategies are unacceptable or refused by the patient or their family. This has already been used for infections of other devices, such as in aortic prostheses for example.[13] Of the studies specifically addressing long-term suppression in PJIs, only two documented the median age, which was 66 and 77 years, respectively.[9,10] The present study is the first to address patients over 80 years of age and is the largest series to date with a

Table 3
Agents used for chronic suppression in 38 patients with prosthetic joint infections (low-dose oral antibiotic therapy)

Agents used for oral PSAT	Daily dosage	Number of patients (%)	Microorganism (number of patients treated)
Amoxicillin	1000 mg tid	14 (37)	*Streptococcus spp* (7), *Enterococcus faecalis* (2), *Campylobacter fetus* (2), *Propionibacterium acnes* (3)
Cloxacillin	1000 mg tid	10 (26)	MS *Staphylococcus aureus* (6), MS coagulase-negative Staphylococcus (4)
Clindamycin	600 mg tid	8 (21)	MS *Staphylococcus aureus* (3), MR *Staphylococcus aureus* (2), MR coagulase-negative Staphylococcus (1), *Finegoldia magna* (1), *Campylobacter fetus* (1)
TMP–SMX	800 mg–160 mg bid	3	MR *Staphylococcus aureus* (1), *Enterobacter cloacae* (1), *Citrobacter koseri* (1)
Fusidic acid[a]	500 mg tid	2	MS *Staphylococcus aureus* (1), MR *Staphylococcus aureus* (1)
Doxycycline	100 mg bid	1	MR *Staphylococcus aureus* (1)

PSAT, prolonged suppressive antibiotic therapy; tid, three times daily; bid, twice daily; MS, methicillin-susceptible; MR, methicillin-resistant; TMP–SMX, trimethoprim–sulfamethoxazole.
[a] Fusidic acid is not recommended as single therapy.

description of their medical condition and the indications for PSAT. This strategy was used in a third of the patients aged ≥80 years in our centre. Joint arthroplasty has low morbidity and mortality, but mostly in very elderly patients (≥80 years) in our experience.[12] At the beginning of the study, a limited surgical procedure was systematically performed to reduce the bacterial burden. However, over time this was performed less often and only in cases with a voluminous abscess, large sinus tract, or uncontrolled sepsis. Thus our study differs from others: only a few patients had undergone surgery, in contrast to previous studies in which all patients had undergone surgical debridement.[8–10] Indeed, we have described the frailest of the oldest patients; their median age was 10 years above that of the patients included in the study by Rao et al.[10] Most of them had major co-morbidities, predominantly cardiovascular diseases (84%), and half of them had an ASA score of 3. Moreover, 14 had already had one or more infections at the same surgical site, which contributed to the decision not to operate further.

One of the strengths of our study is the documentation of the bacteria using deep sampling, excluding patients for whom the diagnosis was made by surface swab sampling or sinus tract culture. Arthrocentesis and synovial fluid analysis showed that most of the bacteria were quite sensitive, allowing oral treatment. The bacterial distribution in our series, with staphylococci and streptococci the first aetiologies of PJI, is explained mostly by a large haematogenous origin. The portal of entry was primarily cutaneous, dental, and urinary tract, as also described in the literature.[14] In the present series, 53% of PJIs were due to staphylococci (predominantly MSSA), which is in keeping with other PJI data.[1,15] However this rate is lower than those found in previous studies on PSAT by Segreti et al. and Rao et al., who found staphylococcal infections in up to 83% and 86%, respectively.[9,10]

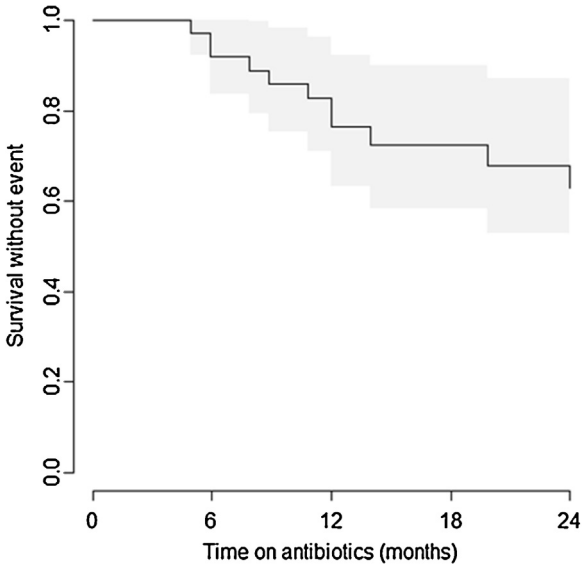

Figure 1. Clinical outcome of 38 patients with prosthetic joint infections treated with prolonged suppressive antibiotic therapy. Kaplan–Meier curve showing survival without event (95% confidence interval in grey). Events are defined as failure and unrelated death.

Treatment failures were most often associated with staphylococci compared to other bacteria, as described previously in the literature.[9,10] Five of six failures were due to *S. aureus* PJI (83%), but only 33% of total *S. aureus* PJI failed. Brandt et al. reported failure in 64% of PJI due to *S. aureus*; these were treated with debridement and retention of the prosthesis.[16] Segreti et al. and Rao et al., on the other hand, demonstrated a good response for PJIs treated with prosthesis retention, with a 69% success rate for *S. aureus* PJI after a mean follow-up of 5 years, using mostly minocycline and rifampin, molecules that achieve high intracellular levels. We did not use these drugs as long-term therapy in our elderly patients because of significant side effects (digestive disorders, enzyme induction). However, we did use doxycycline as a single-therapy once.

Other variables significantly associated with the occurrence of an event were female gender, which may in part be explained by the longer life span of women, the presence of a sinus tract, which has already been associated with treatment failure,[17] and hypoalbuminaemia, which has already been described as being associated with postoperative medical complications in elderly patients with hip fractures.[18] Therefore, optimal nutrition should be achieved in patients on PSAT. The age of the prosthesis and duration of symptoms were not found to be associated with treatment failure, which is in contrast to other studies.

The ideal PSAT regimen has not been established. We treated the great majority of our patients with IV antibiotic therapy for 10 days to 6 weeks, according to the clinical presentation, the bacterial susceptibility, and the treatment outcome. Their treatment was continued with high-dose oral therapy for 4–6 weeks to reduce the bacterial burden and then with a lower dose for prolonged antimicrobial suppression. The doses used for oral antibiotic therapy in PJIs are higher in France than in other countries.[11] We generally used amoxicillin 2 g three times daily for initial oral doses and then 1 g three times daily for the long duration chronic suppression. Osmon et al.[6] recommend oral amoxicillin 500 mg three times daily for chronic oral antimicrobial suppression in streptococcal PJI.

Elderly patients are known to be more at risk of drug-related toxicity,[19] drug interactions, and adherence issues,[20] but antimicrobial adverse events were limited in our experience, since only one patient had to interrupt the treatment. In the absence of a contraindication, beta-lactams were used in 63% of the patients and they were well-tolerated, as reported in other studies.[7–10] In guidelines from the USA, first-generation cephalosporins

Table 4
Univariate assessment of risk factors for treatment failure among patients with prosthetic joint infections treated with prolonged suppressive antibiotic therapy: qualitative variables

Variables	Total number with characteristic	Number of events (%)	Unadjusted HR (95% CI)	*p*-Value[a]
Age, years				
80–85	22	6 (27%)		
≥85	16	9 (56%)	3.87 (1.29–11.62)	0.016
Gender				
Male	17	5 (29%)		
Female	21	10 (48%)	4.55 (1.23–16.74)	0.023
Joint				
Hip	24	11(46%)		
Knee	13	4 (31%)	0.7 (0.22–2.24)	0.549
Shoulder	1	0	-	
Arthroplasty				
Primary implant	24	12 (50%)		
Revised implant	14	3	0.35 (0.10–1.25)	0.105
Gait disorder				
Absent	17	3 (18%)		0.049
Yes	21	12 (57%)	3.62 (1.002–13.05)	
ASA score				
2	17	4 (24%)		
3	21	11 (52%)	2.57 (0.80–8.26)	0.112
Time free of symptoms, months				
<12	14	4 (29%)		
>12	23	10 (43%)	1.20 (0.37–3.93)	0.760
Sinus tract				
Absent	29	9 (31%)		0.020
Yes	9	6 (67%)	3.74 (1.24–11.35)	
Microbiology				
Other bacteria	18	4 (22%)		
Staphylococcus	20	11 (55%)	7.30 (1.61–33.19)	0.010
Bacteraemia				
Absent	29	10 (34%)		
Yes	9	5 (56%)	1.24 (0.38–3.98)	0.722
Surgery				
No	29	8 (28%)		
Yes	9	7 (78%)	2.11 (0.71–6.26)	0.178
Duration of symptoms				
<30 days	15	5 (33%)		
30–90 days	5	2 (40%)	1.18 (0.22–6.53)	0.850
>90 days	18	8 (44%)	1.52 (0.45–5.08)	0.500

HR, hazard ratio; CI, confidence interval; ASA, American Society of Anesthesiologists.
[a] Log-rank test.

(cefalexin and cefadroxil) are preferred for chronic oral antimicrobial suppression,[6] whereas dicloxacillin is recommended as an alternative therapy. In our study, 13% of failures occurred with beta-lactams. All streptococcal infections were treated effectively with amoxicillin. Half of the failures occurred with cloxacillin, but seven patients treated with this molecule had a good outcome with a median duration of cloxacillin of 715 days. However, as mentioned above, we used cloxacillin 1 g three times daily for chronic suppression instead of 500 mg three times daily as per the Infectious Diseases Society of America guidelines. Co-trimoxazole was used three times with two failures and we do not recommend this drug for PSAT. Fusidic acid, which was used twice because of no other therapeutic option, should not be used as a single antimicrobial therapy as this induces bacterial resistance.[21] The suppressive approach is not without risk as the localized septic process can extend and become a systemic infection, but this did not occur in our patients.

One could criticize the use of prolonged antimicrobial agents in the current ecological context, where antimicrobial resistance is a global threat.[22] Faced with the major public health issue of increasing PJIs in aging people,[23] consideration is needed to treat each patient according to the principles of biomedical ethics.[20,24]

Our study is limited by its single-centre retrospective nature and its small size. We did not include patients who received less than 6 months of PSAT. Consequently, we are likely to have underestimated PSAT failures, which is an important bias of our study.

Nevertheless, we can conclude that PSAT is beneficial in selected cases, when surgical excision is contraindicated and when

Table 5
Univariate assessment of risk factors for treatment failure among patients with prosthetic joint infections treated with prolonged suppressive antibiotic therapy: continuous variables

Variables	Total number with characteristic Median (min–max)	Number of events Median (min–max)	Number without event Median (min–max)	Unadjusted HR (95% CI)	*p*-Value[a]
BMI, kg/m^2	35 25.7 (15.8–44.6)	15 23.3 (15.8–44.6)	20 26.3 (17.3–42.8)	0.94 (0.86–1.03)	0.206
Serum albumin, g/l	19 29 (17–41)	8 22 (17–32)	11 31 (17–41)	0.69 (0.54–0.87)	0.019
CRP, mg/l	38 74 (2–600)	15 70 (2–600)	23 77 (3–421)	0.998 (0.993–1.002)	0.299

HR, hazard ratio; CI, confidence interval; BMI, body mass index; CRP, C-reactive protein.
[a] Log-rank test.

the microorganism is susceptible to oral antimicrobial therapy, such as beta-lactams. Prolonged follow-up of the patient and optimal nutrition are recommended, particularly for patients with a staphylococcal infection, with a low serum albumin level, or with a sinus tract.

Larger studies with functional, geriatric, and ecological assessment would be of value to determine the design, the place, and the consequences of PSAT and to better target the patients who would benefit from this treatment.

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